



United States Department of

Health & Human Services

Office of the Assistant Secretary for Preparedness and Response (ASPR)

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# CELL-BASED and RECOMBINANT INFLUENZA VACCINE MANUFACTURING TECHNOLOGIES FOR PANDEMIC INFLUENZA PREPAREDNESS

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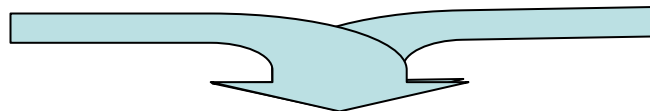
HHS/ASPR/BARDA



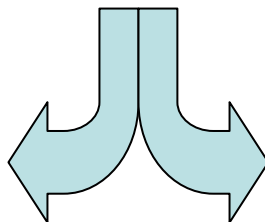




## •Cell-based flu vaccine in the U.S.



Provide incentive to transition from egg-based to more robust cell-based influenza vaccine manufacturing technology, leading to U.S. licensure of new seasonal and pandemic vaccines



CDC/Laura Zambuto





# Cell-based Flu Vaccine



- **Advantages of the cell-based manufacturing technology**
  - Better controlled, less risk of contamination, more expandable
  - Avoids constraints and risks of egg supply
  - Avoids egg allergy
  - May allow isolation of better matched vaccine strains
    - Most of the clinically relevant H3N2 isolates cannot be isolated in eggs (~5%) and therefore considered as vaccine candidates
      - Vaccine mismatch
      - Vaccine delay
      - Vaccine shortage
    - Majority of the H3N2 (>65%) can be isolated in cell culture
  - May have an improved immunological profile over egg-derived vaccine
  - Manufacturing platform will support next generation flu vaccines



# Cell-based Flu Vaccine



- **Development Status**

- Awarded 6 contracts (\$1.3 B) in 2005-06 for advanced development of cell-based seasonal & pandemic influenza vaccines towards US-licensure with commitment for domestic manufacturing surge capacity of 150 M doses in 6 mos. of pandemic onset
- Novartis, Baxter, sanofi pasteur, GSK, Solvay, MedImmune
- Two manufacturers completing Phase 3 clinical studies & expected to submit BLAs in 2010
- Two manufacturers in early stage development
- Two manufacturers down selected in 2009
- One company awarded a follow-on infrastructure building contract





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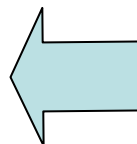
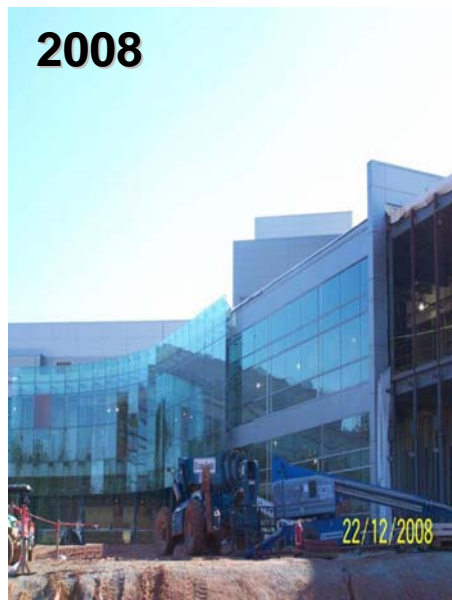
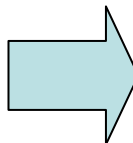
# Infrastructure Building



- In January 2009, HHS awarded a cost-sharing contract to Novartis totaling \$486 M to design and construct a U.S.-based facility with a production surge capacity of at least 150 M doses of pandemic vaccine within 6 months of pandemic onset
  - Must provide at least two commercial-scale lots of influenza or other emerging infectious disease vaccine for up to 20 years
- In November 2009 the facility in Holly Springs, NC opened for MF59 adjuvant production
  - Available for emergency vaccine production by 2011 and expected licensure by 2012-2013



# Infrastructure Building





- **Novartis cell-based influenza vaccine facility, Holly Springs, NC**





- **Obstacles/Challenges**

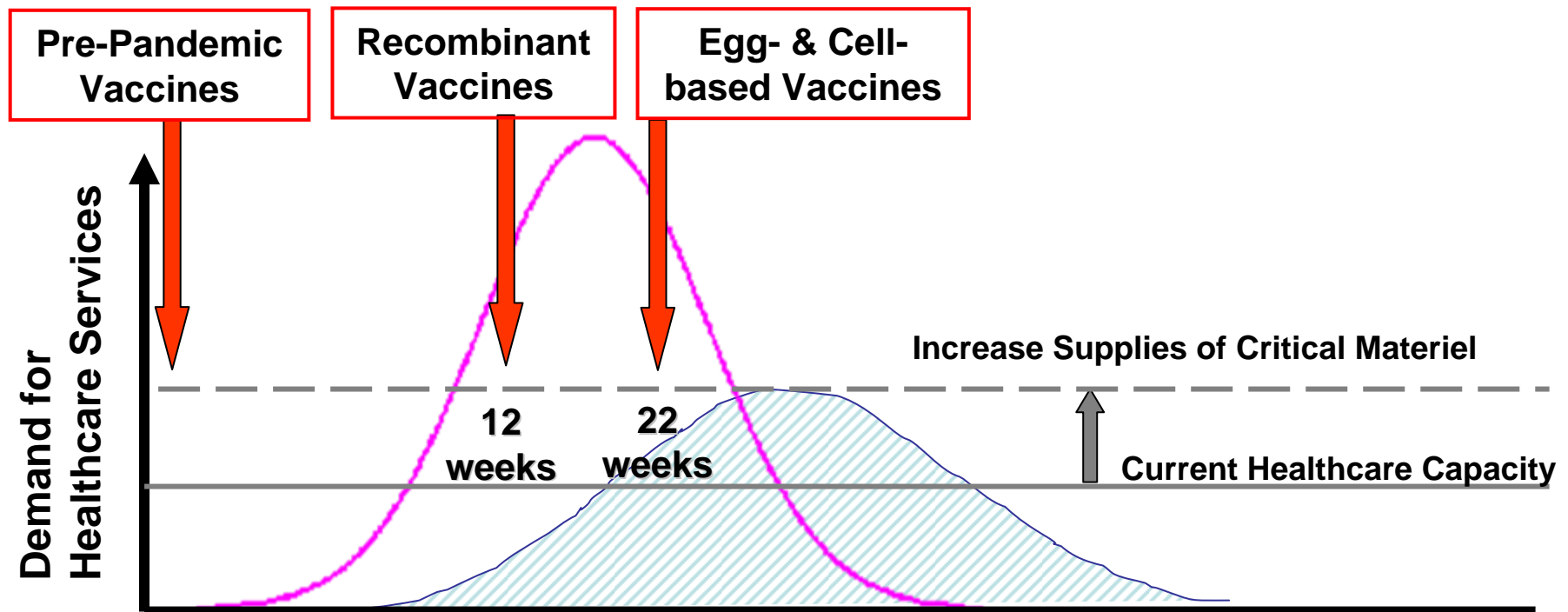
- Manufacturer's concern about "overcapacity"
- Manufacturer's concern over the viability of the business case
  - Large development and infrastructure building costs to realize only evolutionary improvement
- Lack of an accelerated approval process for live, attenuated cell-based influenza vaccine.
- FDA concerns persist about the safety of vaccine (particularly live vaccine) produced in mammalian cell lines
- Comparison of egg- and cell-derived vaccines are complicated by the fact that vaccine seed is derived from eggs
- Value of cell-based strategy investment versus promise of recombinant technologies



## Pandemic Influenza MCM Supply-Demand Gap Closure

Reduce Demand: Pre-Pandemic Vaccines, Community Mitigation, Antivirals, Vaccines, Masks

Increase Capacity: Ventilators, Oxygen, Antivirals, Pandemic Vaccines, Masks,





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# Recombinant Flu Vaccine



- Recombinant & molecular technologies may provide vaccine sooner with less dependence on influenza virus strain properties
- Awarded 1 contract in 2009 (\$155 M) for advanced development of recombinant-based seasonal & pandemic influenza vaccines towards US-licensure with commitment for domestic manufacturing surge capacity of 50 M doses in 6 mos. of pandemic onset & initial lot release in 12 weeks
- Protein Sciences - purified HA protein from baculovirus-derived insect cells
- Completing Phase 3 clinical studies & expected to re-submit BLA in 2010
- RFP issued in Sept. 2009 to support development of additional recombinant & molecular technologies for influenza vaccines with contract awards expected in 2010





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# Recombinant Flu Vaccine



- **Obstacles/Challenges**

- Only a few companies have demonstrated feasibility in phase 1 clinical trials
- Commercially unproven technologies in development at small cap companies

- **Discussion Question**

- How are these technologies translatable to the developing world?



## Contributor Acknowledgements

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